REMARKS

Claims 14, 15, 17-24, 34-38, 40-43, 49-51, 55-65, and 67-69 are pending. No new matter has been added.

Rejection under 35 U.S.C. § 112, first paragraph - written description

Claims 14, 15, 17-24, 34-38, 41-43, 49-51, 55-65, and 67-69 have been rejected under 35 USC § 112, first paragraph, as failing to comply with the written description requirement. According to the Examiner, the as-filed specification fails to describe a method of *in vivo* treating yeast and fungal infections by topically applying *Bacillus coagulans* strain 31284 to skin or to mucous membrane. (*See* Office Action at page 2.) The Examiner states, "[t]he as-filed specification only describes compositions with the cells belonging to some generic representative of the species of *Bacillus coagulans* (page 27-28; formulation 1 and 4) as intended to control fungal and yeasts infections (examples 4, 5, and 7 at pages 29, 31, and 33)." (Office Action at page 2.)

The Synopsis of Application of Written Description Guidelines states that if an amended claim adds additional limitations not present in the original claim and there is express, or inherent, or implicit support for the claim as a whole, the claim meets the written description requirement. (*See* page 6.)

Claims 14, 34, and 49, from which the remaining claims depend, directly or indirectly, were amended in Applicants' July 10, 2006 Amendment and Response ("the July 10, 2006 Response") to the January 19, 2006 Final Office Action to require *Bacillus coagulans* Hammer (ATCC# 31284). Support for this amendment can be found at page 7, lines 20-24; page 10, lines 23 through page 11, line 3; page 11, lines 18-21; and at page 12, lines 6-9. Moreover, the specification states, "The results described herein were obtained with *B. coagulans* Hammer obtained from the American Type Culture Collection (ATCC# 31284) which was grown as described herein and stored in lyophilized aliquots at -20°C." (Specification at page 12, lines 6-9.)

To satisfy the written description requirement, an Applicant must convey with reasonable clarity to those skilled in the art as of the filing date that he or she was in possession of the invention as claimed, i.e., that the disclosure must reasonably convey to the artisan that the inventor has possession of the invention as claimed (MPEP at 2163.02). As is set forth above, Applicants

have provided a detailed description of the claimed invention in the specification. Applicants submit that the written description requirement has been met and that this rejection should be withdrawn.

Rejection under 35 U.S.C. § 112, first paragraph - enablement

Claims 14-24, 34-43, and 49-69 were rejected under 35 U.S.C. § 112, first paragraph as failing to comply with the enablement requirement. (*See* Office Action at page 3.) The Examiner states that the as-filed application does not enable one skilled in the art to practice the invention without an undue amount of experimentation. In applying this rejection, the Examiner has focused upon five factors summarized by In re Wands, 858 F.2d 731 (1988), the scope of the claims, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability of the art, and the amount of experimentation required to enable one skilled in the art to practice the claimed invention. (*See*, Office action, page 4.) This rejection is traversed.

The scope of the claims.

The Examiner has indicated that the breath of the claims is directed to a method for inhibiting yeast and/or fungal infections including vaginal infections by applying topically to skin or mucous membrane probiotic compositions with *Bacillus* coagulans strain ATCC# 31284. (*See* Office action at page 4.) According to the Examiner, the specification only discloses generic doses and generic protocols of topical administration of generic representatives of the species of *Bacillus coagulans*. (*See* Office Action at pages 4 and 5.) Applicants disagree.

The claims specifically require *Bacillus coagulans* Hammer (ATCC# 31284). The specification states, "[t]he results described herein were obtained with *B. coagulans* Hammer obtained from the American Type Culture Collection (ATCC# 31284) which was grown as described herein and stored in lyophilized aliquots at -20°C." (Specification at page 12, lines 6-8.) Exemplary formulations are described in detail throughout the specification (*e.g.*, page 27, lines 16, 23 and 30; page 28, line 8; page 30, line 9 to page 31, line 5; page 31, line 12 to page 32, line3; page 32, lines 4-14; page 32, line 23 to page 33, line 2; page 33, lines 15-22; page 34, lines 6-12; page 35, lines 21-27; page 36, lines 8-11 and 15-18; and page 37, lines 8-9). In fact, specific ranges and absolute amounts of bacteria or spores to be used in the claimed methods are

described in numerous examples. For this reason, an ordinary practitioner would have no difficulty carrying out the claimed methods.

The Examiner has indicated that the specification only discloses *in vitro* assays of antimicrobial activity of *Bacillus coagulans* ATCC# 31284. The Examiner further states that no animals were used as *in vivo* model systems for inhibiting or treating yeast and/or fungal infections including vaginal infections. (*See* Office Action at page 5.) As noted by the Examiner, the as-filed specification discloses the use of *Bacillus coagulans* Hammer (ATCC# 31284) to inhibit infections of *Trichophyton* species and *Candida* species. (*See, e.g.*, Example 1, pages 24-27.) These data demonstrate the inhibitory effectiveness of the *Bacillus coagulans* Hammer (ATCC# 31284). As stated in the July 10, 2006 Response, a zone of inhibition of microbial growth on a plate is a reliable indicator of growth inhibition on another surface, i.e. skin or mucous membrane of a mammal. The data was obtained using an art-recognized assay system. The Examiner has provided no evidence or reason to believe that this assay would not be indicative of activity of the bacteria on skin or mucous membrane. Moreover, animal data or clinical data is not a requirement of § 112.

According to the MPEP, data generated using *in vitro* assays, or from testing in an animal model or a combination thereof almost invariably will be sufficient to establish therapeutic or pharmacological utility for a compound, composition or process. (*See* MPEP § 2107.03.) If the art is such that a model is recognized as correlating to a specific condition, then the model should be accepted as a correlation unless the Examiner has evidence that the model does not correlate. (*See* MPEP s 2164.02.) Rigorous or exact correlation is not required. Merely a reasonable correlation based on the evidence as a whole is sufficient. (*See e.g.*, *In re Brana*, 34 USPQ2d 1436 (1995)). The *in vitro* data disclosed in the present specification adequately demonstrate the capability of *Bacillus coagulans* Hammer (ATCC# 31284) to inhibit yeast and/or fungal infections on skin or on mucous membrane.

The predictability of the art.

The Examiner has indicated that the cited reference, O'Sullivan *et al.*, teaches that selected probiotic strains must be recognized as generally safe and should be a normal inhabitant of the site of application and/or be capable of surviving and growing at the site of application. The Examiner further states that the specification does not provide information about the

capability of *Bacillus coagulans* ATCC# 31284 to survive and grow in the site of the intended application. According to the Examiner, O'Sullivan *et al.* further state, "[a]dherence to body surfaces **may be** an important prerequisite for the long-term survival of probiotic strains..." (O'Sullivan *et al.* at page 312; emphasis added.) The Examiner cites commonly assigned US Patent 6,461,607 as evidence that vegetative cells of *Bacillus coagulans* representatives do not adhere to epithelial cells. The Examiner additionally cites Fuller *et al.* as evidence that attachment of probiotic strains to epithelial cells is host-specific and states that the ability of *Bacillus coagulans* ATCC# 31284 to adhere to epithelial surfaces is not described in the instant specification. (*See* Office Action at pages 6 and 7.) Applicants disagree.

The specification states that the *Bacillus coagulans* species of the present invention are able to colonize skin and mucous membrane tissues, such as vaginal mucous membrane. (*See* specification at page 7, lines 6-19.) Moreover, US Patent 6,461,607 states, "[w]hile the attachment of probiotics to the gastrointestinal epithelium is an important determinant of their ability to modify host immune reactivity, this is not a universal property of Lactobacilli or Bifidobacteria, nor is it essential for successful probiosis. See e.g., Fuller, R., 1989. *J. Appl. Bacteriol.* 66: 365-378." (*See* US Patent 6,461,607 at col. 2, lines 24-29.) Thus, contrary to the Examiner's contention, adherence to body surfaces is not necessarily a prerequisite for *in vivo* survival and growth of the probiotic strain.

The Examiner has also indicated that the art provides no reasonable expectation of success for claims drawn to inhibiting vaginal infection, citing a passage by Seligman (British J. of Obstetrics and Gynaecology, 1995, 102:763-64), which states that studies of the use of probiotics or of bacilli in the treatment of vaginitis and vaginosis have almost all been limited, uncontrolled, and have given variable results. (*See* Office Action at page 7.) In response, as stated in the July 10, 2006 Response, Applicants note that Seligman also cites a study in which the use of *L. acidophilus* successfully controlled candidal vaginitis (Hilton *et al.* Annals Int. Med. 116:353-57, 1992). Thus, contrary to the Examiner's assertion, the state of the art provides a reasonable expectation of success.

As described above, the as-filed specification discloses the use of *Bacillus coagulans* Hammer (ATCC# 31284) to inhibit infections of *Trichophyton* species and *Candida* species. (*See, e.g.*, Example 1, pages 24-27.) These data confirm the predictability of the claimed methods using an experimental system that is well-recognized in the art: zones of inhibition of

microbial growth on culture plates. Thus, the claimed methods do not require the selection of a *Bacillus* species. Given the scope of the claims and the guidance provided in the specification, undue experimentation would not be required to practice the invention.

For the above-stated reasons, Applicants assert that the methods as presently claimed are predictable and that the level of experimentation left to the skilled practitioner is not unnecessary, improper, extensive, or undue. Therefore, the pending claims, as amended herein, are fully enabled, and this rejection should be withdrawn.

CONCLUSION

On the basis of the foregoing amendments and remarks, Applicants respectfully submit that this paper is fully responsive and that the pending claims are in condition for allowance. Such action is respectfully requested. If there are any questions regarding these amendments and remarks, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

Respectfully submitted,

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